

# Bone disease in chronic epilepsy: fit for a fracture

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**Valorisation**



## Valorisation

### Relevance

Worldwide about 65 million people are estimated to have epilepsy.<sup>1</sup> In the Netherlands the prevalence of active epilepsy is approximately 84.000.<sup>2</sup> The majority of the patients diagnosed with epilepsy can expect to achieve good control of seizures with antiepileptic drugs. However, chronic use of antiepileptic drugs is not uncommon. A substantial minority of the patients will continue to experience seizures in spite of several antiepileptic drugs used in adequate doses over longer periods (sometimes decades).

Living with epilepsy is often a great burden for the patients themselves and those around them. Epilepsy sometimes results in significant disability, social exclusion and stigmatisation. People with epilepsy frequently encounter problems in several areas such as education, employment, driving, personal development, psychiatric and psychological aspects and social and personal relationships.<sup>3,4</sup>

In Europe, the annual cost of epilepsy is 15.5 billion.<sup>5</sup> In 2011 direct medical costs in the Netherlands were 248 million ( 0.3% of the health care budget).<sup>6</sup> The three main cost drivers are health care professional visits and hospitalisation (122 million), followed by institutionalised patients (73.6 million) and cost of medication (36.5 million).<sup>6</sup>

Most patients with epilepsy need long-term treatment with anti-epileptic drug(s) (AEDs). Side-effects of antiepileptic drugs can be acute or chronic. The negative influence of antiepileptic drug (AED) use on bone health is classified as a chronic side-effect. In the Dutch guideline on epilepsy 2006 active screening for possible side-effects during antiepileptic drug therapy was advised. However, no specific advice was given for screening measures on bone health. In the update of the Dutch epilepsy guideline in 2011 advices concerning bone health are given. However, these advices are restricted to patients with epilepsy above the age of 50 years using enzyme-inducing AEDs and/or valproate. Considering the body of evidence of the negative influence of AEDs on bone health in our population it seems not justified to restrict these advices to the older patients with epilepsy.

Till this thesis, in the Netherlands no data were available about the prevalence of osteopenia and osteoporosis nor of the vitamin D status in patients with refractory epilepsy. Probably more relevant are our data showing the effect of long-term AED use on the clinical end parameters bone mineral density and fractures. These data are obligatory to develop further guidelines for prevention of bone disease and to the development of protocols for surveillance and treatment of AED associated osteoporosis in the Netherlands.

Moreover, to date the Dutch Osteoporosis Foundation and the Dutch League against Epilepsy have not yet focused their attention on the prevention of metabolic bone disease as a result of chronic AED treatment. In the Netherlands, the estimated

fracture incidence is about 5 pro mille, which means that in one year at least 420 to 500 patients with epilepsy have a bone fracture of any kind. It is not unlikely that, in agreement with a 2-6 times higher fracture risk in patients with epilepsy,<sup>7</sup> the actual incidence of fractures is outnumbered in patients using chronic AEDs.

It has been shown that in adults and children with epilepsy and AEDs use vitamin D supplementation increases BMD significantly.<sup>8,9</sup> Supplementation of 800 IU vitamin D in combination with calcium has proven to be effective in the reduction of fracture risk, especially hip fractures.<sup>10,11</sup> The annual costs of treatment with 1 dd 800 IE cholecalciferol and 1 dd 1 gram calcium are estimated at around € 90 and just around € 54 for vitamin D alone. The direct costs of a spontaneous fracture of a vertebrae or forearm fracture are estimated at around € 1000 per year, for a hip fracture the direct costs are around € 12,000<sup>12</sup> not counting the secondary costs due to loss of working capacity. Therefore, research and in the end development of guidelines for screening and treatment for metabolic bone disease in patients with epilepsy at high risk seems reasonable and cost effective. At this moment osteopenia and later on osteoporosis as a result of long-term AED use is an underestimated problem in patients of all ages, which theoretically can be quite easily prevented or treated.

### Target groups

The results of this thesis are of interest for all physicians who have patients with epilepsy under their attendance. Not only neurologists and child neurologists but also general practitioners, physicians specialised in patients with intellectual disability, internist-endocrinologists and paediatricians. Also orthopaedic surgeons and emergency physicians, who are confronted with the clinical relevant aspects of low BMD, i.e. fractures, should know about the association between AED use and fractures. Nowadays antiepileptic drugs are also used in the psychiatric field and in the treatment of neuropathic pain. Therefore also psychiatrists and physicians specialised in pain-medicine should also be aware of the negative effects of AEDs use on bone health.

However, the results of this these are most relevant for patients with epilepsy themselves. They should be informed about the possible negative influence of AED use on their bone health. In most patients with epilepsy AED treatment is first choice treatment. Therefore monitoring bone health and discussing bone health promoting activities should be common clinical practice when starting AED treatment.

### Activities/ products

The research described in this thesis have led to the identification of low BMD in 80% of the patients and almost 90% prevalence of low 25-OH vitamin D levels. All the patients with osteoporosis and vitamin D deficiency or insufficiency were treated. In all patients with low BMD (osteopenia and osteoporosis) bone health counselling was done by their treating physicians.

## Innovation

To our knowledge this is the first research done in the Netherlands in which a very large population of patients with refractory epilepsy and chronic AED use is screened for low BMD and is analysed for identification of risk factors for low BMD.

## Implementation

There are plans to perform a new screening round for low BMD for all patients with AED use of the long-stay department of Providentia/Kempenhaeghe, in whom 5 years ago osteopenia or normal BMD was diagnosed. Patients with osteoporosis are already under follow-up of an internist-endocrinologist.

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